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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,826	09/07/2000	Axel Ullrich	205884	1983

7590 11/19/2003

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/600,826

Applicant(s)

ULLRICH ET AL.

Examiner

Joseph F Murphy

Art Unit

1646

-- **Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 33-66 is/are pending in the application.
- 4a) Of the above claim(s) 33-46 and 55-65 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 66 is/are allowed.
- 6) ☒ Claim(s) 47-54 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Formal Matters***

Applicant's amendment filed on 8/14/2003 is not compliant with the requirements set forth under 37 CFR 1.121 as amended on June 30, 2003 (see 68 Fed. Reg. 38611, June 30, 2003). Withdrawn claims should be indicated as (Withdrawn) not (Original). However, the amendment has been entered and considered. Claims 33-66 are pending. Claims 33-46, 55-65 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 47-54, 66 are under consideration.

### ***Response to Amendment***

Applicant's arguments filed 8/14/2003 have been fully considered but they are persuasive in part.

The objection to the Specification for non-compliance with the sequence rules has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 47-54 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 47-54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 47-54 under 35 U.S.C. 102(b) as being anticipated by Neilson et al. (1996), has been obviated by Applicant's amendment and is thus withdrawn.

Remaining issues are set forth below.

***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-54 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid which has been deposited as Gene Bank Accession X57205 (Specification at 9), and the polypeptide which is encoded by the deposited nucleic acid, does not reasonably provide enablement for a nucleic acid encoding an FGFR-4 polypeptide or a mutant FGFR-4 polypeptide, an FGFR-4 polypeptide, or a mutated FGFR-4 polypeptide, for reasons of record set forth in the Office Action of 3/11/2003. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record set forth that claims 47-54 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides that will retain the characteristics of FGFR-4 activity. Applicant argues that the methods set forth in the Examples can be used to identify other mutations that result in overexpression in a human cell or tyrosine kinase activity in a human cell that differs from the expression characteristic of wild-type FGFR-4. Assaying for overexpression of a receptor and differential tyrosine kinase activity are within

the ordinary skill in the art and are a matter of routine experimentation, and that it is well established that routine experimentation does not constitute undue experimentation. However, Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass methods using polypeptides which the specification only teaches one skilled in the art to test for functional variants to be used in the claimed method. It would require undue experimentation for one of skill in the art to make and use the claimed polynucleotides, since the skilled artisan would have to first make polypeptide variants of FGFR-4, then test for function. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of FGFR-4. Because the amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely

complex, accurate predictions of a polypeptide's structure from mere sequence data are limited. Thus, since Applicant has only taught how to test for encoded polypeptide variants of FGFR-4, and has not taught how to make polypeptide variants of FGFR-4, it would require undue experimentation of one of skill in the art to make and use the claimed polynucleotides.

Claims 47-54 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 3/11/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to a nucleic acid encoding an FGFR-4 polypeptide or a mutant FGFR-4 polypeptide, an FGFR-4 polypeptide, or a mutated FGFR-4 polypeptide. Applicant argues that the methods set forth in the Examples can be used to identify other mutations that result in overexpression in a human cell or tyrosine kinase activity in a human cell that differs from the expression characteristic of wild-type FGFR-4. Assaying for overexpression of a receptor and differential tyrosine kinase activity are within the ordinary skill in the art and are a matter of routine experimentation. However, The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or

other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides claimed. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed: there is no guidance in the art as to what the defining characteristics of the polypeptides might be. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the molecules that are overexpressed in human cells.

### ***Conclusion***

Claims 47-54 are rejected.

Claim 66 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

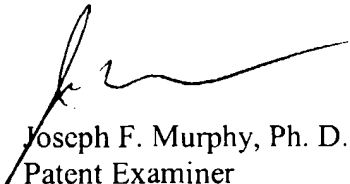
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Advisory Information***


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
November 6, 2003



WONNE EYLER, PH.D.  
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